

FIGURE 1

mAb	Mean Fluorescence Intensity		% Gated	
	L1.2-CCR5	PBMC	L1.2-CCR5	PBMC
mouse IgG1	10	4	1	1
2D7	75	29	92	36
PA8	48	9	73	3
PA9	79	5	96	3
PA10	80	8	96	5
PA11	107	8	96	10
PA12	115	8	96	8
PA14	81	14	96	22

FIGURE 2

INHIBITOR COMBINATION	CONCENTRATION RATIO	ASSAY	COMBINATION INDEX	
			90% Inhibition	50% Inhibition
PA12:2D7	10:1	Entry	0.043	0.291
	2:1	Fusion	0.017	0.019
	10:1	Fusion	0.087	0.067
	50:1	Fusion	0.158	0.046
PA12:PA14	10:1	Entry	0.437	0.535
	10:1	Fusion	0.22	0.263
PA14:2D7	1:1	Entry	2.85	1.85
	1:1	Fusion	1.34	1.74
PA12:PA11	1:1	Entry	0.707	0.641
PA12:RANTES	1000:1	Fusion	0.331	0.156
PA14:RANTES	100:1	Fusion	1.6	1.37
2D7:RANTES	100:1	Fusion	0.972	0.962
PA12:CD4-IgG2	10:1	Fusion	0.3	0.31
PA14:CD4-IgG2	1:1	Fusion	0.957	0.566
2D7:CD4-IgG2	1:1	Fusion	1.127	0.302

FIGURE 3

	Epitopes	IC ₅₀ values (μg/ml)			
		cell-cell fusion inhibition	viral entry inhibition	gp120-binding inhibition	calcium flux inhibition
PA8	Nt	-	-	-	-
PA9	Nt/ECL2	-	-	0.24	-
PA10	Nt/ECL2	-	-	0.13	-
PA11	Nt	25.5	-	0.33	-
PA12	Nt	10.0	-	0.24	-
PA14	Nt/ECL2	1.7	.024	1.58	6.4
2D7	ECL2	1.6	.026	1.38	45

	1								5							10						15						20						25						30					
Nt	M	D	Y	Q	V	S	S	P	I	Y	D	I	N	Y	Y	T	S	E	P	C	Q	K	I	N	K	Q	I	A	A	A	R														
2D7	X	92	54	90	nd	83	63	82	nd	46	40	X	40	90	90	86	111	49	57	45	44	37	X	52	27	92	X	X	X	X	65														
PA8	X	118	63	78	nd	52	36	32	nd	4	-2	X	0	53	-2	45	100	47	32	56	44	57	X	54	-24	134	X	X	X	X	36														
PA9	X	-16	-13	0	nd	213	-19	-13	nd	10	-0	X	-19	62	52	29	73	36	32	36	45	30	X	55	-18	145	X	X	X	X	40														
PA10	X	-21	-14	0	nd	175	59	-22	nd	14	-8	X	-15	101	48	49	94	27	47	45	45	39	X	53	-13	133	X	X	X	X	46														
PA11	X	70	32	0	nd	112	80	81	nd	40	-22	X	51	74	70	46	85	32	47	56	48	40	X	47	-22	146	X	X	X	X	44														
PA12	X	68	30	0	nd	76	81	51	nd	34	-12	X	49	76	68	40	86	30	41	49	46	34	X	54	-12	93	X	X	X	X	43														
PA14	X	9	86	75	nd	85	88	89	nd	57	40	X	64	78	84	66	76	80	71	44	86	64	X	76	46	99	X	X	X	X	33														

	90						95						100					
ECL1	H	Y	A	A	A	Q	W	D	F	G	N	T	M	C	Q			
2D7	70	89	X	X	X	40	130	40	66	X	58	72	82	0	74			
PA8	38	92	X	X	X	49	118	32	115	X	96	86	68	-10	39			
PA9	51	66	X	X	X	27	81	-16	159	X	138	89	57	0	43			
PA10	67	83	X	X	X	36	139	-18	133	X	112	97	61	0	40			
PA11	59	81	X	X	X	38	91	-25	78	X	60	94	71	-10	60			
PA12	63	67	X	X	X	35	91	29	77	X	76	79	102	-25	55			
PA14	73	79	X	X	X	63	83	-23	86	X	47	89	80	-8	77			

	170						175						180						185						190					
ECL2	R	S	Q	K	E	G	L	H	Y	T	C	S	S	H	F	P	Y	S	Q	Y	Q	F	W	K	N	F	Q			
2D7	62	55	17	0	X	X	X	62	64	65	0	83	95	51	52	32	80	92	73	42	34	73	39	33	45	102				
PA8	38	40	58	31	X	X	X	65	43	63	26	90	100	51	41	46	90	69	74	59	38	95	33	40	27	62				
PA9	39	28	63	15	X	X	X	34	13	0	29	93	112	27	43	27	79	63	75	74	13	51	38	17	35	59				
PA10	45	59	34	19	X	X	X	30	-21	0	25	84	96	32	61	39	77	82	53	68	-16	59	45	16	58	70				
PA11	67	58	45	33	X	X	X	49	138	130	17	78	95	40	48	38	91	99	61	54	-24	73	47	23	50	92				
PA12	52	56	36	31	X	X	X	52	102	136	59	73	85	44	49	42	101	90	45	56	-23	66	37	28	55	74</				



FIGURE 5A

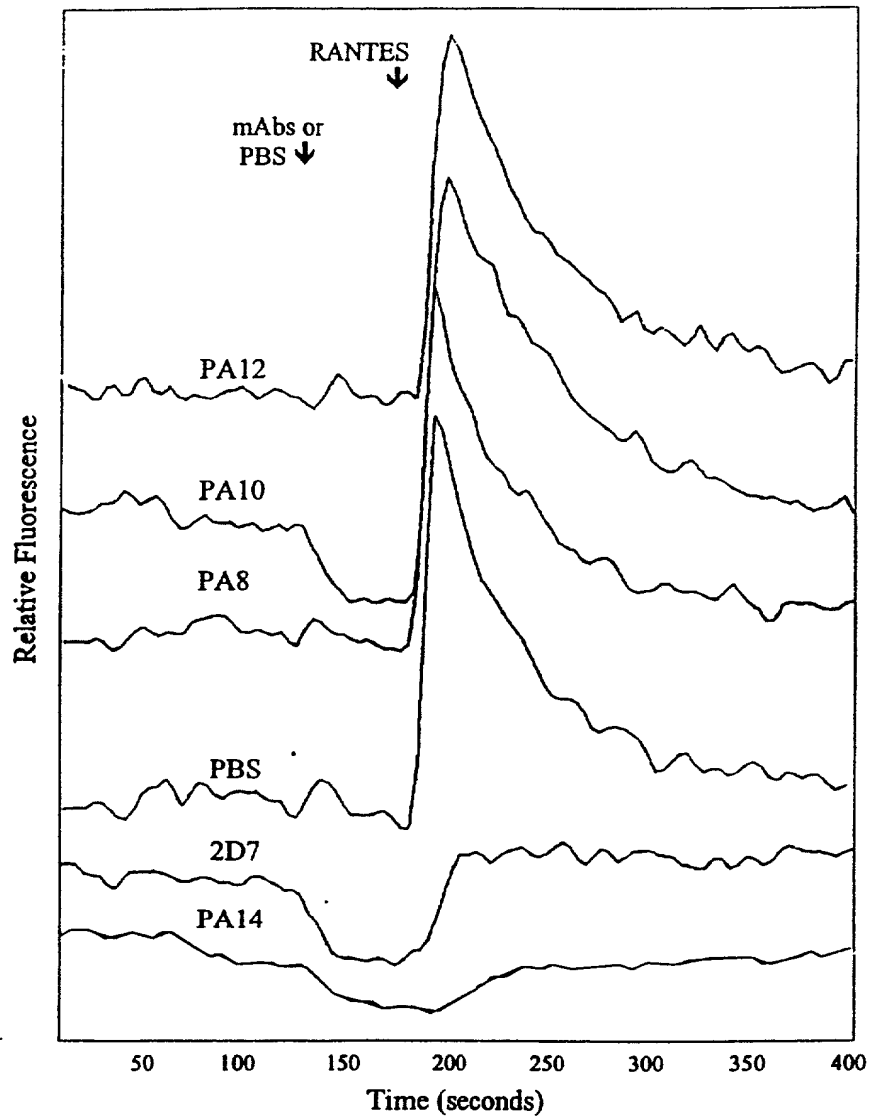


FIGURE 5B

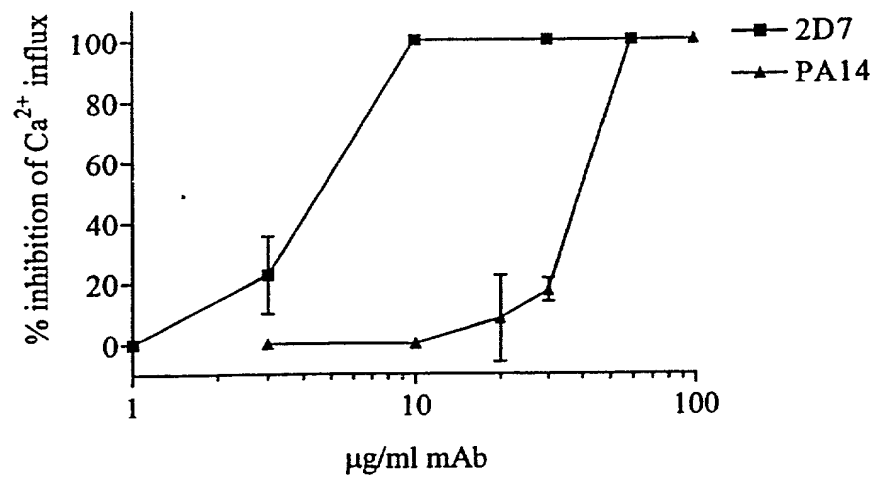


FIGURE 6A

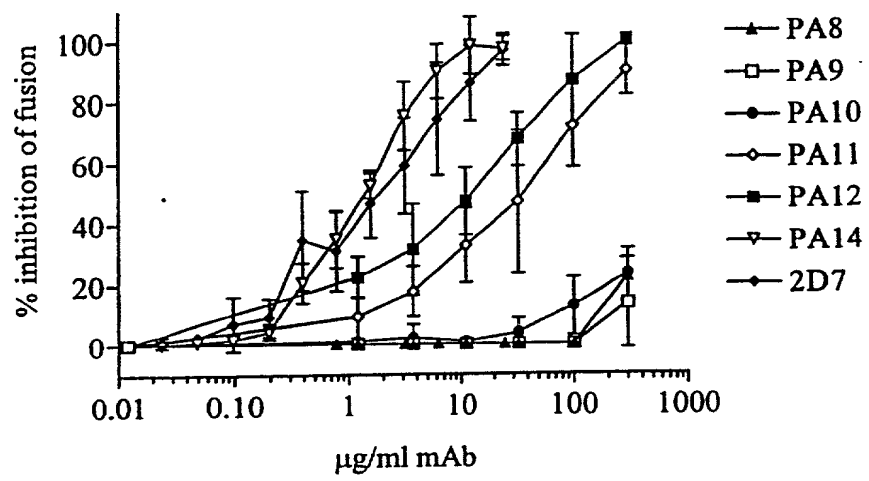


FIGURE 6B

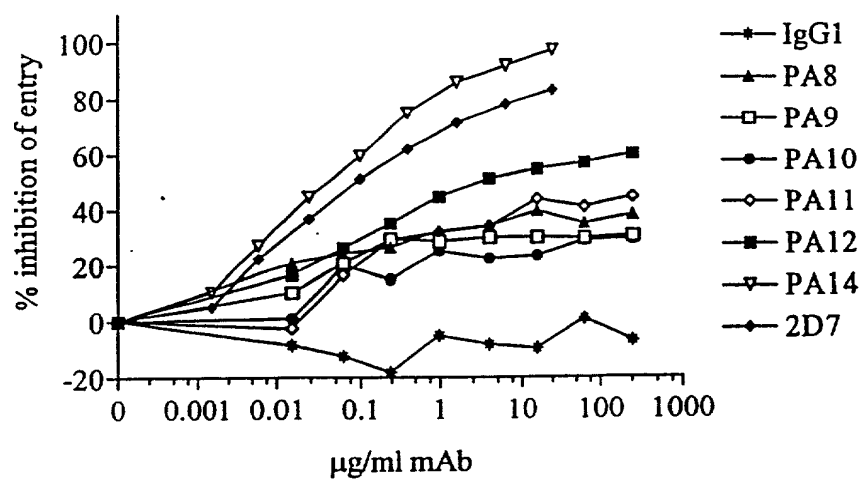


FIGURE 6C

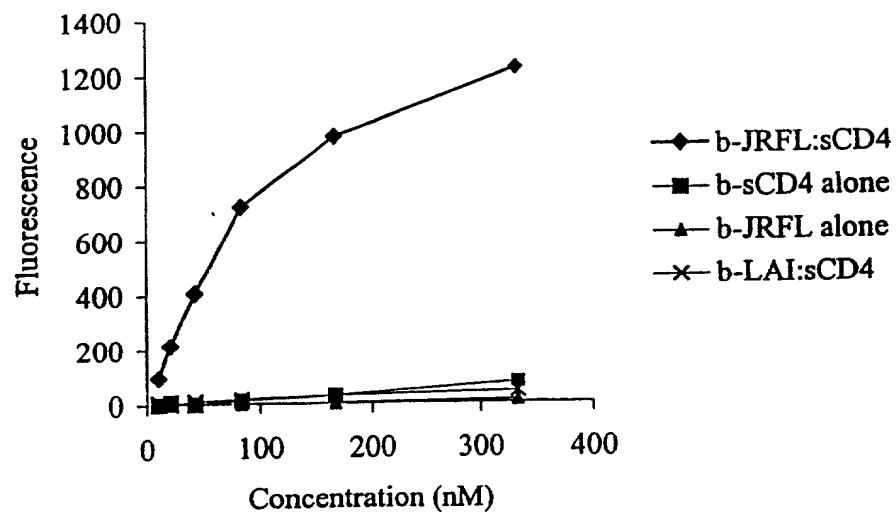


FIGURE 6D

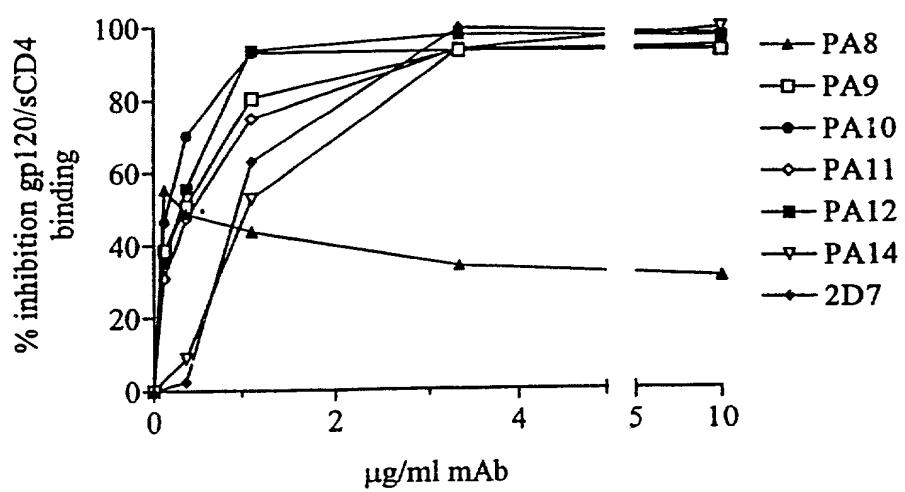
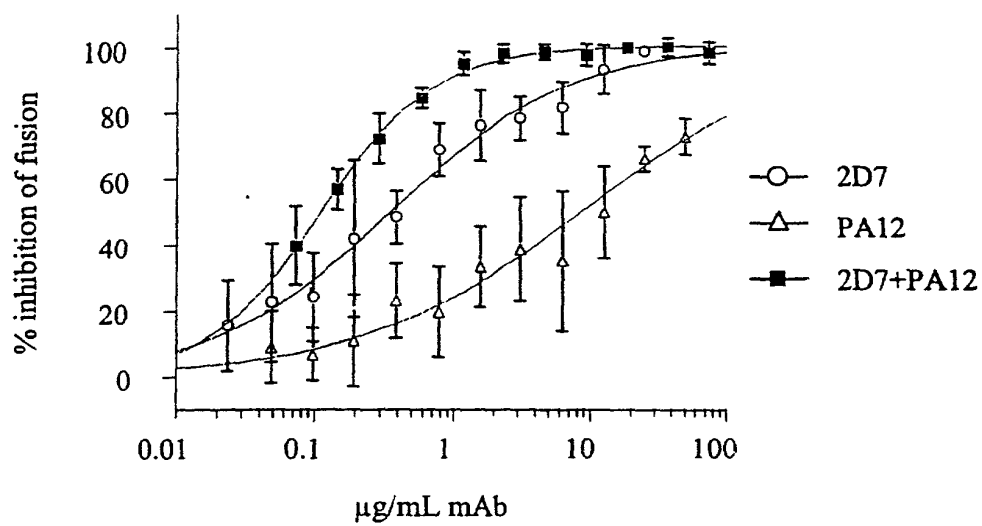


FIGURE 7



12/20 12/20 12/20

FIGURE 8

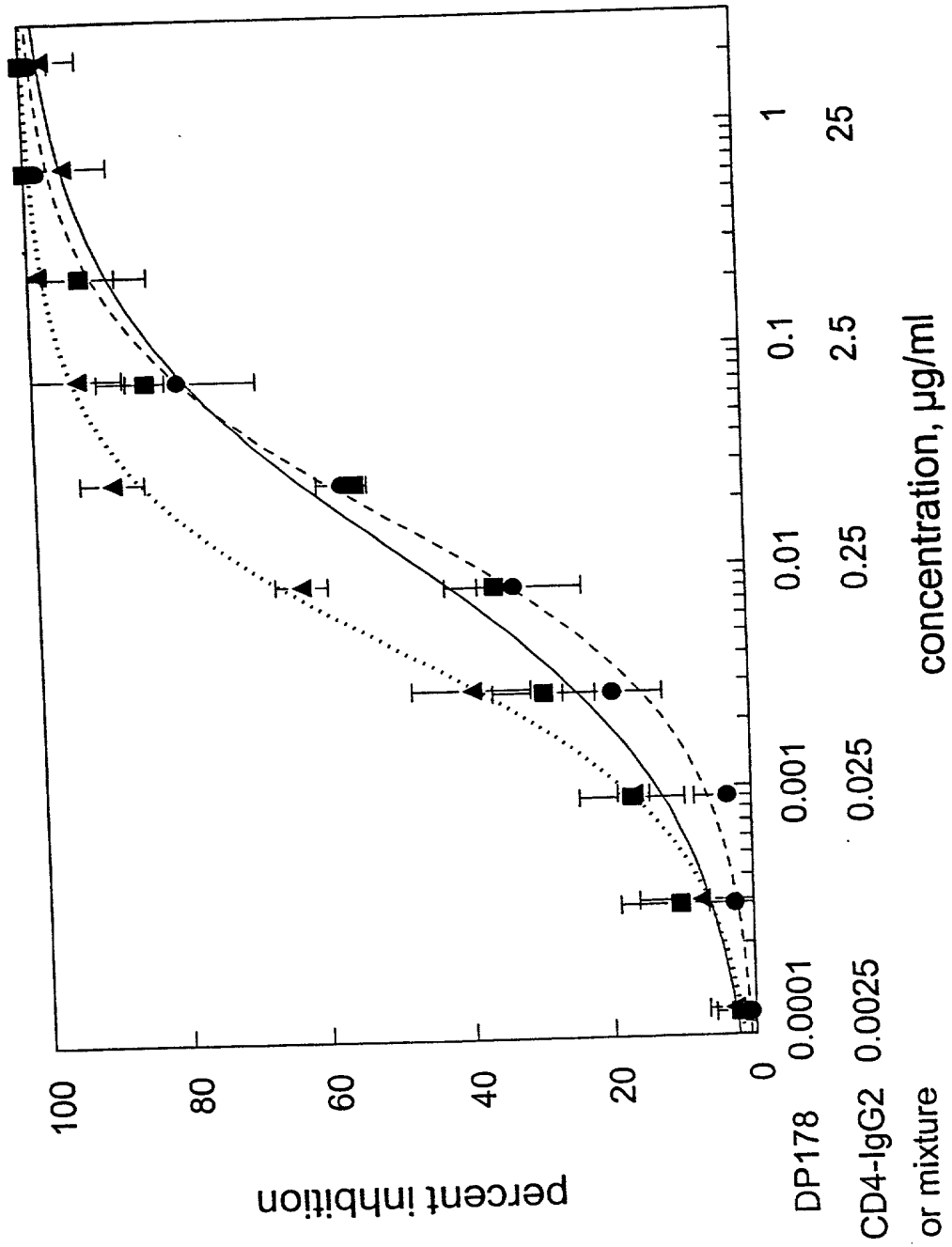


FIGURE 9

Percent Inhibition	Combination Index			
	CD4-IgG2:T-20 Mass Ratio			
	25:1 (low)	25:1 (high)	5:1	1:1
95	0.32	0.20	0.22	0.50
90	0.38	0.25	0.27	0.55
85	0.43	0.29	0.30	0.59
80	0.47	0.33	0.34	0.62
75	0.51	0.36	0.37	0.65
70	0.54	0.39	0.40	0.67
65	0.58	0.42	0.43	0.70
60	0.61	0.45	0.45	0.73
55	0.65	0.48	0.49	0.75
50	0.69	0.51	0.52	0.78

Percent Inhibition	T-20			CD4-IgG2		
	Concentration, $\mu\text{g/ml}$		Dose Reduction	Concentration, $\mu\text{g/ml}$		Dose Reduction
	Alone	Combination		Alone	Combination	
99	1.1	0.17	6.6	130	4.3	29
95	0.21	0.044	4.9	19	1.10	17
90	0.10	0.024	4.2	7.8	0.59	13
70	0.025	0.0076	3.3	1.6	0.19	8.4
50	0.011	0.0039	2.8	0.60	0.095	6.3

FIGURE 11A

Percent Inhibition	Combination Index	PRO 542				PA12				T-20			
		Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction	
95	0.41	10	2.1	4.8	730	2.8	260	94	19	4.9			
90	0.45	7.0	1.6	4.4	320	2.1	150	63	14	4.5			
70	0.47	4.1	0.92	4.5	72	1.2	60	30	8.1	3.7			
50	0.48	3.1	0.66	4.7	28	0.87	32	19	5.8	3.3			

PRO 542, PA12 and T-20 were used in an approximate 1:1:10 molar concentration ratio.

T-09070" 3T932350

FIGURE 11B

		PRO 542				PRO 140				T-20			
Percent Inhibition	Combination Index	Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction	
		Alone		Mix		Alone		Mix		Alone		Mix	
95	0.40	8.5	1.9	4.5	19	1.0	19	1.0	19	140	17	8.2	
90	0.39	7.1	1.5	4.7	13	0.77	17	0.77	17	100	13	7.7	
70	0.37	5.3	0.87	6.1	7.2	0.46	16	0.46	16	57	7.7	7.4	
50	0.35	4.6	0.63	7.3	4.9	0.34	14	0.34	14	40	5.6	7.1	

PRO 542, PRO 140 and T-20 were used in an approximate 2:1:20 molar concentration ratio.

FIGURE 11C

		PRO 542				PRO 140				T-20			
Percent Inhibition	Combination Index	Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction	
		Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix
95	0.24	61	2.5	24	2.5	11.9	0.72	17	156	22	7.1		
90	0.22	32	1.4	23	8.4	0.40	21	96	13	7.4			
70	0.19	9.8	0.50	20	4.5	0.14	32	40	4.5	8.9			
50	0.18	4.7	0.26	18	3.0	0.074	41	23	2.3	10			

PRO 542, PRO 140 and T-20 were used in an approximate 4:1:30 molar concentration ratio.

FIGURE 11D

Percent Inhibition	Combination Index	PRO 140				T-20			
		Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction	
		Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix
95	0.56	12	1.8	6.7	156	55	2.8		
90	0.55	8.4	1.1	7.4	96	35	2.7		
70	0.55	4.5	0.51	8.8	40	16	2.5		
50	0.56	3.0	0.31	9.9	23	10	2.4		

PRO 140 and T-20 were used in an approximate 1:30 molar concentration ratio.

Triple Combination Synergistically Blocks HIV-1 Entry (1)

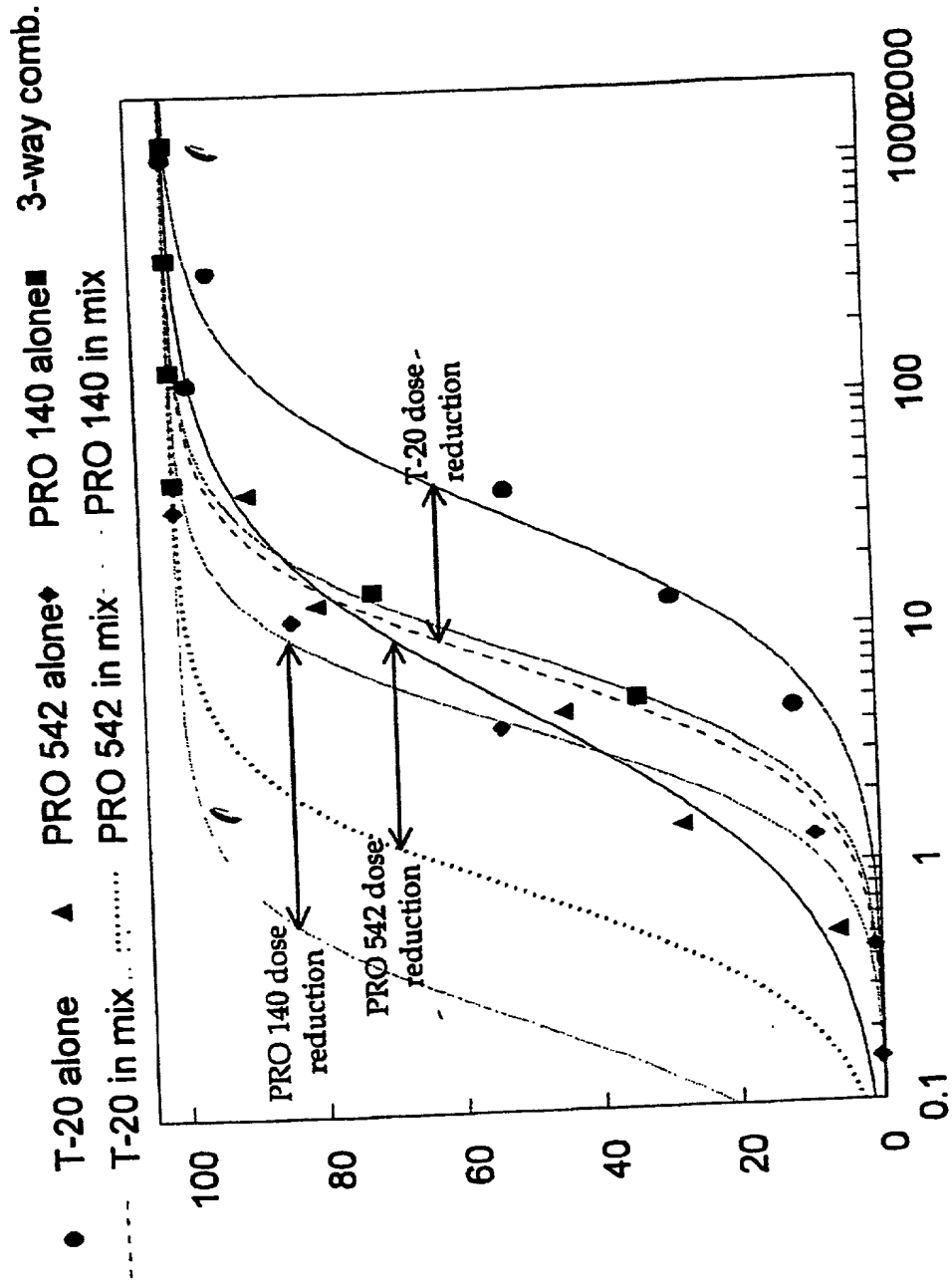


FIGURE 13 ST 992860

